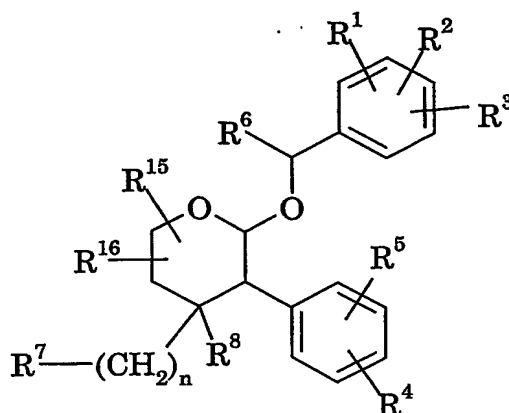


**CLAIMS**

1. A compound of formula (I):



(I)

5

wherein

R<sup>1</sup> is hydrogen, halogen, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, fluoroC<sub>1-6</sub>alkyl, fluoroC<sub>1-6</sub>alkoxy, C<sub>3-7</sub>cycloalkyl, C<sub>3-7</sub>cycloalkylC<sub>1-4</sub>alkyl, NO<sub>2</sub>, CN, SR<sup>a</sup>, SOR<sup>a</sup>, SO<sub>2</sub>R<sup>a</sup>, CO<sub>2</sub>R<sup>a</sup>, CONR<sup>a</sup>R<sup>b</sup>, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl or C<sub>1-4</sub>alkyl substituted by C<sub>1-4</sub>alkoxy, wherein R<sup>a</sup> and R<sup>b</sup> each independently represent hydrogen or C<sub>1-4</sub>alkyl;

R<sup>2</sup> is hydrogen, halogen, C<sub>1-6</sub>alkyl, fluoroC<sub>1-6</sub>alkyl or C<sub>1-6</sub>alkoxy substituted by C<sub>1-4</sub>alkoxy;

R<sup>3</sup> is hydrogen, halogen or fluoroC<sub>1-6</sub>alkyl;

R<sup>4</sup> is hydrogen, halogen, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, fluoroC<sub>1-6</sub>alkyl, fluoroC<sub>1-6</sub>alkoxy, hydroxy, NO<sub>2</sub>, CN, SR<sup>a</sup>, SOR<sup>a</sup>, SO<sub>2</sub>R<sup>a</sup>, CO<sub>2</sub>R<sup>a</sup>, CONR<sup>a</sup>R<sup>b</sup>, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl or C<sub>1-4</sub>alkyl substituted by C<sub>1-4</sub>alkoxy, wherein R<sup>a</sup> and R<sup>b</sup> are as previously defined;

R<sup>5</sup> is hydrogen, halogen, C<sub>1-6</sub>alkyl, fluoroC<sub>1-6</sub>alkyl or C<sub>1-6</sub>alkoxy substituted by C<sub>1-4</sub>alkoxy;

R<sup>6</sup> represents hydrogen or a C<sub>1-4</sub>alkyl group optionally substituted by a hydroxy group;

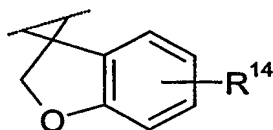
R<sup>7</sup> represents a 5- or 6-membered carbonyl or sulfonyl containing cyclic group comprising from 0 to 3 nitrogen ring atoms, from 0 to 1 oxygen ring atom

25

- and from 0 to 1 sulfur ring, wherein said ring is optionally substituted at any substitutable position by one or more substituents selected from =O, halogen, hydroxy, R<sup>11</sup>, R<sup>12</sup>, SR<sup>f</sup>, SO<sub>2</sub>R<sup>g</sup>, COR<sup>a</sup>, CO<sub>2</sub>R<sup>a</sup>, CONR<sup>9</sup>R<sup>10</sup>, -ZNR<sup>9</sup>R<sup>10</sup>, benzyl, C<sub>1-4</sub>alkyl, hydroxyC<sub>1-4</sub>alkyl, fluoroC<sub>1-4</sub>alkyl, chloroC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxyC<sub>1-4</sub>alkyl, C<sub>3-7</sub>cycloalkyl, C<sub>3-7</sub>cycloalkylC<sub>1-4</sub>alkyl, C<sub>3-7</sub>cycloalkoxy, C<sub>3-7</sub>cycloalkoxyC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, fluoroC<sub>1-4</sub>alkoxy, hydroxyC<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkoxyC<sub>1-4</sub>alkoxy, aryl, arylC<sub>1-4</sub>alkyl, heteroaryl, heteroarylC<sub>1-4</sub>alkyl or a 5- or 6-membered ring containing in the ring one oxygen atom or N(C<sub>1-6</sub>alkyl), wherein R<sup>f</sup> is C<sub>1-4</sub>alkyl or aralkyl or aryl and R<sup>g</sup> is C<sub>1-4</sub>alkyl, aryl, arylC<sub>1-4</sub>alkyl or NR<sup>9</sup>R<sup>10</sup>;
- 10 R<sup>8</sup> represents hydrogen, C<sub>1-6</sub>alkyl, fluoroC<sub>1-6</sub>alkyl, hydroxy, C<sub>1-6</sub>alkoxy, hydroxyC<sub>1-6</sub>alkyl NR<sup>9</sup>R<sup>10</sup>, CONR<sup>9</sup>R<sup>10</sup> or SO<sub>2</sub>R<sup>g</sup>;
- R<sup>9</sup> is hydrogen, C<sub>1-4</sub>alkyl, C<sub>3-7</sub>cycloalkyl, C<sub>3-7</sub>cycloalkylC<sub>1-4</sub>alkyl, fluoroC<sub>1-4</sub>alkyl, C<sub>2-4</sub>alkyl substituted by a C<sub>1-4</sub>alkoxy or hydroxyl group, or R<sup>9</sup> is a five membered or six membered nitrogen-containing heteroaromatic ring as
- 15 previously defined;
- R<sup>10</sup> is hydrogen or C<sub>1-4</sub>alkyl, C<sub>3-7</sub>cycloalkyl, C<sub>3-7</sub>cycloalkylC<sub>1-4</sub>alkyl, fluoroC<sub>1-4</sub>alkyl or C<sub>2-4</sub>alkyl substituted by a C<sub>1-4</sub>alkoxy or hydroxyl group;
- or R<sup>9</sup>, R<sup>10</sup> and the nitrogen atom to which they are attached form a heteroaliphatic ring of 4 to 7 ring atoms, optionally substituted by one or two
- 20 groups selected from hydroxy, COR<sup>e</sup>, CO<sub>2</sub>R<sup>e</sup>, C<sub>1-4</sub>alkyl optionally substituted by a C<sub>1-4</sub>alkoxy or hydroxyl group, or C<sub>1-4</sub>alkoxy optionally substituted by a C<sub>1-4</sub>alkoxy or hydroxyl group, or a five membered or six membered nitrogen-containing heteroaromatic ring as previously defined, or said heteroaliphatic ring is substituted by a spiro-fused lactone ring, and said heteroaliphatic ring optionally
- 25 containing a double bond, which heteroaliphatic ring may optionally contain an oxygen or sulphur ring atom, a group S(O) or S(O)<sub>2</sub> or a second nitrogen atom which will be part of a NH or NR<sup>d</sup> moiety, where R<sup>d</sup> is C<sub>1-4</sub>alkyl optionally substituted by hydroxy or C<sub>1-4</sub>alkoxy;
- or R<sup>9</sup>, R<sup>10</sup> and the nitrogen atom to which they are attached form a
- 30 non-aromatic azabicyclic ring system of 6 to 12 ring atoms;
- or R<sup>9</sup>, R<sup>10</sup> and the nitrogen atom to which they are attached form a heteroaliphatic ring of 4 to 7 ring atoms to which is fused a benzene ring or a five membered or six membered nitrogen-containing heteroaromatic ring optionally containing 1, 2 or 3 additional heteroatoms selected from N, O and S;

$R^{11}$  and  $R^{12}$  each independently represent hydrogen, hydroxy,  $COR^e$ ,  $CO_2R^e$ ,  $C_{1-4}$ alkyl optionally substituted by a  $C_{1-4}$ alkoxy or hydroxyl group, or  $C_{1-4}$ alkoxy optionally substituted by a  $C_{1-4}$ alkoxy or hydroxyl group;

or, when they are attached to the same carbon atom,  $R^{11}$  and  $R^{12}$  may together represent  $=O$ ,  $=CHCO_2R^a$ ,  $-O(CH_2)_mO-$ ,  $-CH_2O(CH_2)_k-$ ,  $-CH_2OCH_2C(O)-$ ,  $-CH_2OCH_2CH(OH)-$ ,  $-CH_2OCH_2C(CH_3)_2-$ ,  $-CH_2OC(CH_3)_2CH_2-$ ,  $-C(CH_3)_2OCH_2CH_2-$ ,  $-CH_2C(O)OCH_2-$ ,  $-OC(O)CH_2CH_2-$ ,  $-C(O)OCH_2CH_2-$ ,  $-C(O)OC(CH_3)_2CH_2-$ ,  $-C(O)OCH_2C(CH_3)_2-$ ,  $-OCH_2(CH_2)_k-$ ,  $-OC(CH_3)_2CH_2CH_2-$ ,  $-OCH_2C(CH_3)_2CH_2-$ ,  $-OCH_2CH_2C(CH_3)_2-$ ,  $-OCH_2CH=CHCH_2-$ ,  $-OCH_2CH(OH)CH_2CH_2-$ ,  $-OCH_2CH_2CH(OH)CH_2-$ ,  $-OCH_2C(O)CH_2CH_2-$ ,  $-OCH_2CH_2C(O)CH_2-$ , or a group of the formula



or, where they are attached to adjacent carbon atoms,  $R^{11}$  and  $R^{12}$  may together represent  $-OCH_2CH_2-$  or  $-OCH_2CH(OH)-$ , or  $R^{11}$  and  $R^{12}$  may together form a fused benzene ring;

or,  $R^{11}$  and  $R^{12}$  together form a  $C_{1-2}$ alkylene bridge across the pyrrolidine, piperidine, morpholine or piperazine ring to which they are attached;

$R^{13}$  represents hydrogen, phenyl, benzyl, pyridyl, tetrahydropyranyl, piperidinyl, N-substituted piperidinyl (where the N-substituent is  $C_{1-6}$ alkyl),  $C_{1-4}$ alkyl,  $C_{3-7}$ cycloalkyl,  $C_{3-7}$ cycloalkyl $C_{1-4}$ alkyl,  $-SO_2C_{1-4}$ alkyl or  $C_{2-4}$ alkyl substituted by a  $C_{1-4}$ alkoxy or hydroxyl group;

$R^{14}$  represents hydrogen, halogen, hydroxy,  $C_{1-4}$ alkyl, hydroxy $C_{1-4}$ alkyl or fluoro $C_{1-4}$ alkyl;

$R^{15}$  and  $R^{16}$  each independently represent hydrogen, halogen,  $C_{1-6}$ alkyl,  $CH_2OR^c$ , oxo,  $CO_2R^a$  or  $CONR^aR^b$  where  $R^a$  and  $R^b$  are as previously defined and  $R^c$  represents hydrogen,  $C_{1-6}$ alkyl or phenyl;

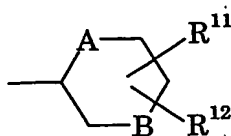
Z represents a bond,  $C_{1-6}$ alkylene or  $C_{3-6}$ cycloalkylene;

k is 1, 2 or 3;

m is 1 or 2; and

n is zero, 1 or 2;

with the proviso that when n is zero and R<sup>8</sup> is hydrogen, R<sup>7</sup> does not represent a C-linked nitrogen-containing ring of the formula



5

wherein

A represents NR<sup>13</sup>, and B represents a bond, CH<sub>2</sub>, NR<sup>13</sup> or O, wherein one or both hydrogen atoms in said CH<sub>2</sub> moiety may be replaced with one or both of R<sup>11</sup> and R<sup>12</sup>, or alternatively, one of the hydrogen atoms in said CH<sub>2</sub> moiety together with a hydrogen atom from an adjacent carbon are replaced by a double bond; or A is O, and B is NR<sup>13</sup>; and R<sup>11</sup> and R<sup>12</sup> together represent =O; and pharmaceutically acceptable salts thereof.

2. A compound according to Claim 1 wherein R<sup>1</sup> is hydrogen, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, halogen or CF<sub>3</sub>.

3. A compound according to Claim 1 or Claim 2 wherein R<sup>2</sup> is hydrogen, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, halogen or CF<sub>3</sub>.

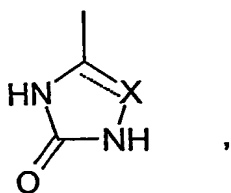
4. A compound according to any one of Claims 1 to 3 wherein R<sup>3</sup> is hydrogen, fluorine, chlorine or CF<sub>3</sub>.

5. A compound according to any one of Claims 1 to 4 wherein R<sup>4</sup> is hydrogen or fluorine.

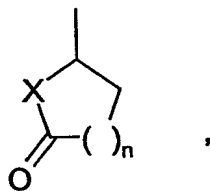
6. A compound according to any one of Claims 1 to 5 wherein R<sup>5</sup> is hydrogen, fluorine, chlorine or CF<sub>3</sub>.

7. A compound according to any one of Claims 1 to 6 wherein R<sup>6</sup> is C<sub>1-4</sub>alkyl optionally substituted by hydroxy.

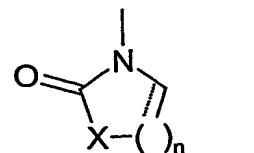
8. A compound according to any one of Claims 1 to 7 wherein  $R^7$  is a cyclic group selected from the group consisting of:



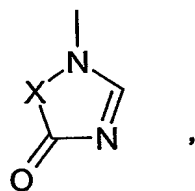
X is N, CH or  $CH_2$



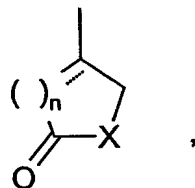
X is O or  $CH_2$   
n is 1 or 2



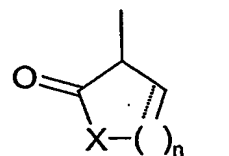
X is O, NH,  $CH_2$  or  $NR^{13}$   
n is 1 or 2



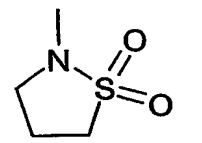
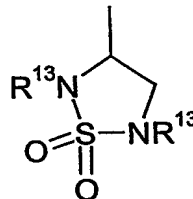
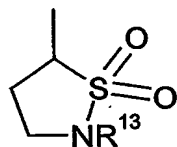
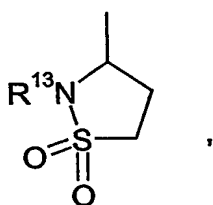
X is NH or  $CH_2$



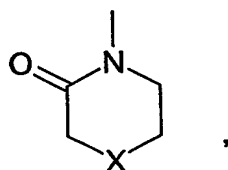
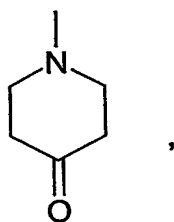
X is O, NH,  $CH_2$  or  $NR^{13}$   
n is 1 or 2



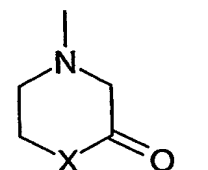
X is O, NH,  $CH_2$  or  $NR^{13}$   
n is 1 or 2



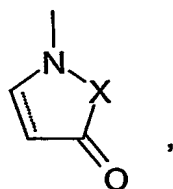
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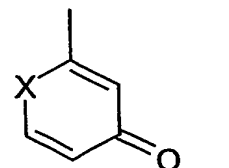
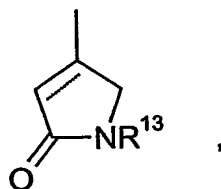
X is  $NR^{13}$  or  $CH_2$



X is  $NR^{13}$  or  $CH_2$

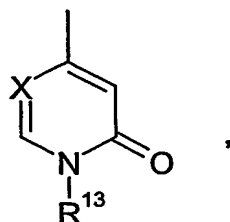
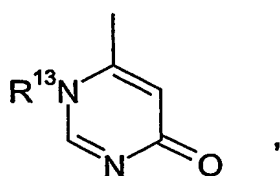


X is  $NR^{13}$  or  $CH_2$

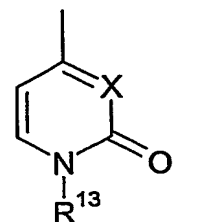


X is  $NR^{13}$ , O or  $SO_2$

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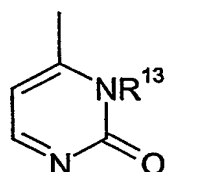
X is N or CH



X is N or CH



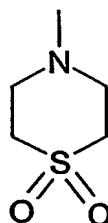
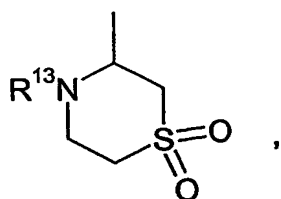
and



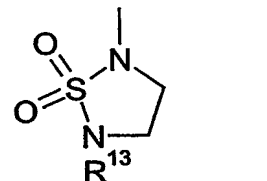
X is N or CH

wherein  $R^{13}$  is as defined in Claim 1, and further wherein any of said cyclic groups is optionally substituted by one or more groups as defined in Claim 1.

- 5            9.        A compound according to any one of Claims 1 to 7 wherein  $R^7$  is a cyclic group selected from the group consisting of:



and



- 10            wherein  $R^{13}$  is as defined in Claim 1, and further wherein any of said cyclic groups is optionally substituted by one or more groups as defined in Claim 1.

- 10            10.        A compound according to any one of Claims 1 to 9 wherein  $R^8$  is hydrogen or methyl.

- 15            11.        A compound according to any one of Claims 1 to 10 wherein  $R^{12}$  is hydrogen, hydroxy,  $C_{1-2}$ alkyl substituted by hydroxy,  $C_{1-4}$ alkoxy or  $CO_2R^e$  (where  $R^e$  is hydrogen, methyl ethyl or benzyl).

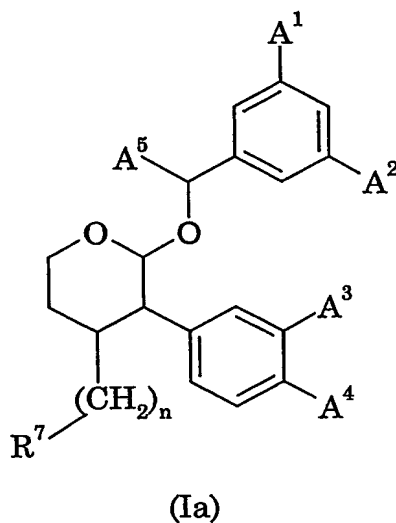
12. A compound according to any one of Claims 1 to 11 wherein  $R^{13}$  represents hydrogen, methyl or ethyl.

5 13. A compound according to any one of Claims 1 to 12 wherein  $R^{15}$  and  $R^{16}$  are both hydrogen atoms.

14. A compound according to any one of Claims 1 to 13 wherein n is zero or 1.

10

15. A compound according to Claim 1 of the formula (Ia):



15 wherein

$A^1$  is fluorine or  $CF_3$ ;

$A^2$  is fluorine or  $CF_3$ ;

$A^3$  is fluorine or hydrogen;

$A^4$  is fluorine or hydrogen;

20  $A^5$  is methyl; and

$R^7$  and n are as defined in Claim 1;

or a pharmaceutically acceptable salt thereof.

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16. A pharmaceutical composition comprising a compound according to any one of Claims 1 to 15, together with at least one pharmaceutically acceptable carrier or excipient.

5 17. A compound according to any of claims 1 to 15 for use in a method of treatment of the human body.

18. A method for the treatment or prevention of physiological disorders associated with an excess of tachykinins, which method comprises  
10 administration to a patient in need thereof of a tachykinin reducing amount of a compound according to Claim 1.

19. A method for the treatment or prevention of pain or inflammation, migraine, emesis, postherpetic neuralgia, depression or anxiety, which method  
15 comprises administration to a patient in need thereof of a therapeutically effective amount of a compound according to Claim 1.

20. Use of a compound as claimed in any one of Claims 1 to 15 for the manufacture of a medicament for the treatment or prevention of physiological  
20 disorders associated with an excess of tachykinins.

21. Use of a compound as claimed in any one of Claims 1 to 15 for the manufacture of a medicament for the treatment or prevention of pain or inflammation, migraine, emesis, postherpetic neuralgia, depression or anxiety.  
25